REMARKS

The Office Action dated April 7, 2011 has been reviewed carefully and Claim 1, the sole independent claim, has been amended so as to more precisely recite unique aspects of the invention. Reconsideration of the rejection of original Claims 1 through 11 and allowance of the same are respectfully requested.

The Invention

The present invention has solved a problem in respect of treating preeclampsia which can become eclampsia, a life-threatening condition. The present invention treats the pregnant patient by administering a therapeutically effective dosage of metolazone, which dosage is less than a diuretic dose of metolazone, This is recited in Claim 1.

Dependent Claims 3 and 4 recite, respectively, administering the dose orally and administering the dose in solid dose form.

A significant feature of the invention is set forth in dependent Claim 5 which recites the treatment being effective without adversely affecting the fetus. Claim 6 further recites that the treatment is effected without substantial volume reduction in the intravascular extracellular fluid.

Dependent Claim 7 recites administering as said dosage of metolazone about 0.04mg/kg bodyweight.

Dependent Claims 8 and 9 deal with the repeated administration and frequency thereof. Claim 10 recites the patient being a human being.

Claim 11 recites administering as said dosage about 2 to 2.5 mg/day.

Claims 1-11 – Section 103(a)

These claims were rejected on the basis of Raghunathan in view of McCarty. Claim 2 has been cancelled.

Raghunathan was cited as teaching that metolazone is an antihypertensive agent.

Raghunathan is directed toward a dry mixture of a drug having a reduced particle size being employed to create dosage preparations which provide rapid dissolution and increased bioavailability of drugs having low water solubility. It is noted that metolazone is a diuretic and an antihypertensive agent which has the problem of poor water solubility. Neither Applicant nor Raghunathan has made a claim to having invented metolazone. Raghunathan's objective was to

provide metolazone in a form which would dissolve rapidly, thereby improving bioavailability. There is no departure from any conventional use of the medication in terms of diuretic or antihypertensive uses or variations from conventional dosage.

McCarty focuses on the use of magnesium taurate for the prevention and treatment of preeclampsia and eclampsia. It lists at the reference location "column 2, lines 9-15" standard prior art treatments for pre-eclampsia which are said to include bed rest, intravenous magnesium sulfate, antihypertensive drugs and induction of early labor. The prime focus of McCarty is the use of magnesium taurate in the prevention and treatment of preeclampsia and eclampsia. There is no specific reference to metolazone, but rather merely a generic reference to antihypertensive drugs. There is further no teaching or suggestion of employing a reduced dosage of a diuretic or doing so to effect the treatment without adversely affecting the fetus (Claim 5) or effecting treatment without substantial volume reduction in intravascular extracellular fluid (Claim 6). There is also no teaching of Applicant's preferred dosage of metolazone in Claim 7 (about 0.04mg/kg bodyweight), or Claim 11 (about 2 to 2.5mg/day).

Considering the combination of Raghunathan and McCarty, it is respectfully submitted that they are directed towards different problems and cannot be combined without significant destruction of the individual teachings. More specifically, Raghunathan employs as an example the diuretic and antihypertensive agent metolazone in dealing with the objective of enhancing water solubility of a pharmaceutical. There is no aspect of his disclosure which deals with preeclampsia or potential adverse consequences of the treatment of the same. McCarty, after setting forth the hereinbefore reference prior art standard treatments for preeclampsia, focuses on the use of magnesium taurate which forms no part of the enhanced water solubility objectives of Raghunathan.

Of critical importance when considering these two references is the fact that neither of them, whether considered individually or in combination, contains any reference direct or tangential to Applicant's unique method which employs a therapeutically effective dosage of metholazone administered at a dosage level which is less than a diuretic dose. Raghunathan would employ the conventional dose. In the reference to the prior art contained within McCarty, there is no disclosure indicating any desire to reduce or depart from the standard dosage of antihypertensive drug and there is direct focus on the asserted unique contribution involving the use of magnesium taurate.

It is respectfully submitted that whether considered individually of in combination, the Raghunathan and McCarty references do not render obvious Applicant's invention as set forth in the Claim 1.

Turning to the dependent claims, Claim 5 recites effecting the treatment without adversely affecting the fetus. There is no such teaching of this method aspect which results from the reduced dosage of the diuretic in either applied reference. Similarly, Claim 6 recites effecting the treatment without substantial volume reduction in intravascular extracellular fluid. There is no such teaching or accomplishment in either applied reference. As to dependent Claim 5, which refines the recital of the dosage of metholazone as being about 0.04mg/kg bodyweight, the two prior references are devoid of any such teaching with metholazone merely serving as an example of a compound which could benefit from the enhanced water dissolving characteristics of Raghunathan. There is no use of metholazone or a reduced dosage thereof in McCarty. Similarly, Applicant's Claim 11 recites the preferred dosage of about 2 to 2.5mg/day, which also is no part of either disclosure.

The features of dependent Claims 3, 4, 8, 9 and 10 are not asserted as independently contributing to patentability apart from their dependency directly or indirectly from amended Claim 1.

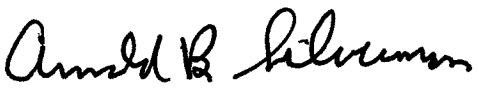
Considering the legal standards applicable to a §103(a) rejection it has been stated, "in determining the differences between the prior art and the claims, the question under 35 U.S.C. § 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious." MPEP 2141.02 *citing*, *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Schenck v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). Additionally, "[a] prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention." MPEP 2141.02(VI), *citing*, *W.L. Gore and Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 US 851 (1984).

"If the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification." MPEP 2143.01(V), *citing*, *In re Gordon*, 733 F.2d 900, 221 UPSQ 1125 (Fed. Cir. 1984). "If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of

the references are not sufficient to render the claims *prima facie* obvious," MPEP 2143.01(VI), *citing*, *In Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959). It is respectfully submitted that modifying either Raghunathan or McCarty to meet the limitations of Applicant's amended Claim 1, would certainly depart from their respective objectives and change their principles of operation and would render them unsatisfactory for their intended purpose.

It is respectfully submitted that Claims 1 and 3-11 are patentable over the applied art and that the application is now in proper form for issuance of a Notice of Allowance. Such action is respectfully requested at an early date.

Respectfully submitted,



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